Anti-n-methyl-d-aspartate receptor encephalitis presenting as postpartum psychosis: A case report

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ABSTRACT

Anti-N-methyl-d-aspartate (NMDA) receptor encephalitis is a form of encephalitis occurring primarily in women and associated with antibodies against NR1 or NR2 subunits of the NMDA receptor. As psychiatric symptoms may predominate at the onset or over the course of the disease, the diagnosis is frequently delayed. Yet, the patients' prognosis depends on the speed with which the disease is detected, identified, and managed. Because the presence of pronounced psychiatric symptoms drives the patients to psychiatric institutions, physicians need to be aware of autoimmune encephalitis and propose the detection of autoantibodies as early as possible to provide optimal medical care to such patients. Here, we report the case of a 24-year-old female who presented to the hospital with symptoms suggestive of postpartum psychosis but further investigations revealed her to be positive for anti-NMDA receptor autoantibodies.

Key words: *Anti-NMDA receptor antibody, Encephalitis, Postpartum psychosis, Pregnancy*

Anti-N-methyl-d-aspartate (NMDA) receptor encephalitis was first described in 2007 when 12 patients presenting with prominent neuropsychiatric symptoms were confirmed to have antibodies to the NMDA receptors in their serum or cerebrospinal fluid (CSF) [1]. Patients with anti-NMDA receptor encephalitis have been reported to have high rates of psychiatric symptoms and clinicians may be unaware of diverse presentations that unfold in this disorder [2]. Acute psychosis in anti-NMDA receptor encephalitis is associated with serum and CSF IgG antibody titers against the NR1a subunit of the receptor. However, antibodies against different antigens (e.g., the NR2a and NR2b subunits) have been described in cases of limbic encephalitis, systemic lupus erythematosus (SLE), and psychiatric symptoms may not be exclusive to the NR1a subunit [3].

Potential causes for the behavior, learning, and memory difficulties in anti-NMDA receptor encephalitis have been postulated to be due to reversible predominant frontotemporal atrophy, an area in which NMDA receptors are present in high density; therefore, suggesting an immunological cause to the atrophy [4]. Here, we report the case of a 24-year-old female who presented to the hospital with symptoms suggestive of postpartum psychosis but further investigations revealed her to be positive for anti-NMDA receptor autoantibodies.

CASE REPORT

A 24-year-old Hindi speaking Muslim female educated until the 5th standard, married and a homemaker, resident of Mumbai and native of Bihar was brought to the emergency department by her relatives in a disheveled state with complaints of irrelevant talk, disrobing in public, angry/abusive/assaultive behavior, and disturbed sleep since the past 5 days. As per the elder sister of the patient, she had delivered a male child 10 days prior through cesarean section and was apparently alright the next 5 days post-cesarean section when she developed sudden onset deviation of angle of the mouth toward the left side with the left-sided weakness.

The patient was taken to a local doctor given some injectable (documentation not available) and advised computerized tomography (CT) scan brain, which was done and revealed no abnormality. Following which, the patient perceived full improvement in the next 24 h. The very next day, the mother noticed a change in her behavior. She started claiming that her husband is having an illicit affair with his sister-in-law and that her in-laws are conspiring to kill her. She would be seen muttering to self-claiming that she could hear voices of her dead relatives who are going to take her to heaven. She would be seen reciting religious hymns at odd hours which she would not do previously. She would be seen gesticulating in air, laughing to self with occasional crying spells.

The symptoms worsened over the next few days and the patient started accusing all her family members of doing black magic on her, would get aggressive try to hit the family members if they tried to reason with her. She started claiming that the newborn child was not hers and that it was conceived from another woman

who had an illicit affair with his husband. She would further state that she could see a black dog with red eyes and sharp teeth roaming inside the house, waiting to bite her following which she would not sleep the entire night, try to run away from the house, disrobe on the road following which she had to be brought back forcefully inside. As she became unmanageable, the family members decided to take her to the emergency for further management.

On further inquiry, there was no history suggestive of similar behavior during the previous childbirth 2 years back. No history suggestive of mania, depression, psychosis, obsessive-compulsive disorder (OCD) or substance use in a dependent pattern was noted. No history of preceding seizure or head injury was there. No significant medical or surgical comorbidity was noted apart from the left-sided weakness 1 day before the onset of symptoms. She was the youngest of five siblings, born of a non-consanguineous marriage, and had no family history of any psychiatric illness. She was presently living with her husband, her daughter, and in-laws in a rented two-room house.

On assessing her premorbid personality, it was revealed that she was extrovert, predominantly cheerful, responsible, religious, and socially well adjusted, liked spending time with family and painting. On systemic examination, her abdomen was soft, sutures were present no other abnormalities were detected. Her pulse and blood pressure were normal. She was seen restrained on admission, disheveled ill-kempt, shouting expletives claiming everyone has colluded to kill her and refused to answer formal queries following which the mental status examination (MSE) was deferred.

The patient was admitted to the ward and a provisional diagnosis of postpartum psychosis was given. Injection lorazepam 4 mg was administered to control her agitation following which she slept. All routine blood investigations were sent along with chest X-ray and electrocardiogram. The patient was started on olanzapine 5 mg twice a day and clonazepam 0.5 mg thrice a day orally. All routine investigations were normal and the patient was kept under observation in the ward and serial MSEs were carried out.

On the 3rd day, the patient became cooperative for MSE, conveyed delusions of persecution and 2nd and 3rd person auditory hallucinations. Her immediate and recent memory was impaired and insight was Grade I. Gradually, the dose of olanzapine was increased and there was a gradual improvement in her symptoms. On the 10th day of admission, her olanzapine was at 20 mg/day in divided doses and clonazepam was made 0.5 mg twice a day. The relatives claimed more than 60% improvement with improved sleep, self-care, and decreased aggression with residual irritability and forgetfulness. She would also ask about her newborn. The MSE revealed persecutory ideas that could be challenged and she claimed decreased auditory hallucination and was not acting out. Her insight had improved to Grade III. The memory deficits persisted, however, with recall being 1/5 and impaired recent memory even on hints; remote memory would be intact. The auditory hallucinations resolved by the 13th day, gynecology reference was done and the patient was planned for discharge in the next few days.

On the 14th day, the patient developed sudden onset spasm of her neck muscles, deviation of angle of the mouth toward the left side and rigidity of both the upper limbs. She had marked slurring of speech, following which all the medications were withheld and injection promethazine 50 mg intramuscular was administered and serum creatine phosphokinase (CPK) levels were measured. There was a marked improvement in the rigidity within the next half an hour and her serum CPK levels were normal (130.8 mg/dl) and she was started on promethazine 25 mg orally twice a day. The next day, on the 15th day of admission, there was mild slurring but no rigidity and promethazine was continued at the same dose. The same evening the patient had an episode of unresponsiveness, followed by frothing, tongue bite, rhythmic movement of all the limbs, and incontinence lasting for around a minute suggestive of a generalized tonic-clonic seizure. An urgent neurology reference was done and she was started with phenytoin 100 mg thrice a day.

A magnetic resonance imaging (MRI) brain was suggested along with CSF assay, EEG, and serum calcium levels. CSF assay could not be done due to the refusal of the caregivers to give consent. EEG and serum calcium were within normal limits; however, her MRI revealed hyperintensities in bilateral parahippocampal regions, bilateral occipital periventricular, and white matter not showing restriction of diffusion. A serum anti-NMDAR antibody titer was advised which came out to be positive following which a diagnosis of anti-NMDAR encephalitis was made.

The patient was planned to be shifted to the neurology ward and to start intravenous immunoglobulins (IVIG). The patient and her relatives refused the same and insisted on discharge as they perceived no behavioral abnormalities then and stated they wanted a second opinion from a private doctor. The risks were explained and the patient was given discharge against medical advice following which the patient did not come for follow-up.

DISCUSSION

Clinical presentations in anti-NMDA receptor encephalitis are heterogeneous and pose a challenge to the clinicians. Some common clinical features that should arouse an index of suspicion in a clinician are: (a) Non-specific prodrome such as headache, low-grade fever, or a viral-like illness (headaches, respiratory, or gastrointestinal symptoms) in the weeks before acute presentation; (b) psychiatric symptoms are prominent such as agitation, bizarre and disinhibited behavior, delusions and auditory, and visual hallucinations; (c) cognitive dysfunction like short-term memory loss can also be a presenting feature, as can concentration difficulties; (d) motor dysfunction in addition to typical epileptic seizures, patients often develop dyskinetic movements, including orofacial dyskinesias (grimacing or lip-smacking), which may be mistaken for seizures, and (e) autonomic instability and hypoventilation can also occur as can cardiac dysrhythmias often necessitating intensive care unit management [5].

Confirmation of the clinical diagnosis of anti-NMDA receptor encephalitis requires a positive serum or CSF sample screening for antibodies to the NMDA receptor subunit [2]. The treatment must target both the cause and the clinical consequences of the encephalitis. With respect to the former, first-line treatment is immunotherapy, typically corticosteroids, IVIG, or plasma exchange. With respect to the immediate management of behavioral and psychotic symptoms, both typical and atypical, antipsychotics have been used [6,7].

A similar case was presented by Ford *et al*. in their study. They reported the case of a 40-year-old African American lady who complaints of sudden onset behavioral changes in the form of inability to complete her normal tasks and being forgetful and not acting like herself. Other complaints include hyper religiosity, intermittent agitation, and insomnia. With the passage of time, she became more disorganized in her speech and expressed paranoid delusions. Gradually, her symptoms worsened and she developed autonomic fluctuations requiring admission to intensive care. Serology confirmed the presence of anti-NMDAR antibodies following which she was administered IVIG, IV corticosteroids, plasmapheresis, and rituximab. The patient was eventually discharged after 130 days with continuous improvement on serial follow-ups [8].

Another case was described of anti-NMDA receptor encephalitis in a 15-year-old Chinese female. She had 1 month history of worsening of mania and memory problems along with mild fever, generalized fatigue, anorexia, and right hand abnormal involuntary movement. Neurological examination showed an irritable patient with impaired short-term memory, echolalia, echopraxia, stereotype movement in her right hand, and oral-facial dyskinesias. On further investigation, her serology was positive for anti-NMDAR antibodies along with evidence of teratoma on abdominal ultrasonography. The patient was administered IVIG for 7 days following which there was a significant improvement in her symptoms, followed by laparoscopic resection of teratoma. The patient was discharged a month later with significant improvement. Her cognitive function was fully recovered and her psychiatric symptom, involuntary movement, sensory disturbance, and oral-facial dyskinesias disappeared 6 months later [9].

In our case, we presented the case of anti-NMDA receptor encephalitis presenting as postpartum psychosis. There was little to arouse an index of suspicion but motor dysfunction along with persisting cognitive dysfunction pointed toward further investigation which revealed the true etiology. The case, however, could not be followed up and the prognosis could not be studied.

CONCLUSION

Thus, any atypical presentation should always be looked for and investigated so that we do not miss any such cases as they have high mortality and morbidity, if left untreated. The atypical heterogeneous presentation even with the realm of routine psychiatric diagnoses must be viewed with suspicion in the light of any neurological overlay and must be investigated to not a miss a diagnosis of anti-NMDA receptor antibody encephalitis. To the best of our knowledge, this is the first case for the presentation of the disorder with postpartum psychosis.

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